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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,742	06/01/2005	Corrado Fogher	GRT/4161-12	1064

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EXAMINER
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WORLEY, CATHY KINGDON

ART UNIT	PAPER NUMBER
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1638

MAIL DATE	DELIVERY MODE
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12/10/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/534,742	<b>Applicant(s)</b> FOGHER, CORRADO	
	<b>Examiner</b> CATHY K. WORLEY	<b>Art Unit</b> 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 August 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 5-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 May 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/12/05; 6/16/05</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Restriction/Election*

1. In response to the communication received on Aug. 29, 2008, from Gary R. Tanigawa, the election with traverse of group II, claims 1-4, as they relate to SEQ ID NO:36, is acknowledged.

The Applicant traverses on the grounds that the technical feature linking the inventions is flours that have low allergenicity made from the seeds of transgenic non-wheat plants (see pages 5-6 of the response filed on Aug. 29, 2008). This is not persuasive, however, because the Examiner has provided references teaching such flours (see restriction requirement mailed on April 29, 2008). The Applicant argues that the two references relied upon by the Examiner can not be combined to demonstrate a lack of inventive step because WO 98/08607 teaches only wheat dough and is directed to viscoelasticity (see pages 6 and 7 of the response). This is not persuasive, however, because the second reference, US Patent No. 6,517,875 teaches non-wheat flours and is directed to properties of flour, including rising of the dough. The Applicant argues that US Patent No. 6,517,875 does not teach any flours that have no wheat flour included (see page 7 of the response). This is not persuasive, however, because there is nothing in the instant claims to exclude the addition of wheat flour to the flour derived from non-wheat seeds. The Applicant

argues that US Patent No. 6,517,875 teaches that the transglutaminase should not be ground and that this teaches away from have the transglutaminase in the seeds that will be processed to produce the flour (see pages 7-8 of the response). This is not persuasive, however, because the claims of US Patent No. 6,517,875 do not exclude including the transglutaminase during grinding, and even if this is not the preferred embodiment of US Patent No. 6,517,875, one of ordinary skill in the art would expect a certain amount of transglutaminase enzyme activity to be retained, even after grinding of the seeds. The Applicant also argues that the references do not teach mutating the allergenic domains of the HMW protein (see second paragraph on page 8 of the response). This is not persuasive, however, because the instant claims state that mutation of the protein is optional, and therefore, this is a limitation that is not present in each of the groups and it can not be the special technical feature that links the groups.

The restriction requirement is proper and is MADE FINAL. Claims 1-12 are pending in the instant application. Claims 5-12 are withdrawn for being directed to non-elected inventions. Claims 1-4 are examined in this Office Action as they relate to SEQ ID NO:36. The Applicant is reminded to amend the claims to recite only the elected sequence of SEQ ID NO:36.

The Applicant is reminded that when the examiner has required restriction between product and process claims, and where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn

process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

***Information Disclosure Statement***

2. The Information Disclosure Statement (IDS) filed on June 16, 2005, has been considered. The IDS filed on May 12, 2005, has been considered, however, references which were in a foreign language were lined through, because no translation has been provided. Where an English abstract was available, the Examiner considered the English abstract and added "ABST" to the IDS to indicate that only the English abstract had been considered. Furthermore, the International Search Reports were considered, however, they were lined through by the Examiner because they are not appropriate for printing on the front of an issued patent. These search reports were considered even though they have been lined through.

3. The listing of references in the specification on page 17 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

***Specification***

4. The abstract of the disclosure is objected to because it is not sufficiently descriptive of the invention. The abstract should be between 50 and 150 words in length and it should specify that transgenic non-wheat plants expressing wheat glutenins and transglutaminase are utilized. New matter must be avoided, therefore the Applicant is advised to utilize language that is present in the originally filed specification. Correction is requested. See MPEP § 608.01(b).

5. The title of the invention is not descriptive of the elected invention. A new title is required that is clearly indicative of the invention to which the claims are directed. The new title should specify that transgenic non-wheat plants expressing wheat glutenins and transglutaminase are utilized.

***Claim Objections***

6. Claims 1-4 are objected to because of the following informalities:

- Claims 1-3 continue to recite non-elected embodiments; for example, claim 1 has the word “optionally”, however, the Applicant has elected the invention in which SEQ ID NO:36 has been modified by mutagenesis; and also, the claims continue to recite non-elected sequences.

- Claim 4 is technically incorrect, because it recites "wherein the cereal plant is rice soybean or corn", however soybeans are not cereals, therefore, this recitation is technically incorrect.

Appropriate correction is requested.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in these rejections.

The term "low allergenic" in claim 1 is a relative term which renders the claim indefinite. The term "low allergenic" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Does this mean less allergenic than flour from a different plant species? Does this mean less allergenic than flour from a non-transgenic plant of the same species? Does this mean less allergenic for a particular population of people? For the purpose of examination, this recitation will be interpreted to encompass any flour that is less allergenic than any other flour for any individual who may



consume it. This interpretation does not relieve the Applicant of the need to address this rejection under 35 USC 112, 2<sup>nd</sup> paragraph.

The term "rising" in claim 1 is a relative term which renders the claim indefinite. The term "rising" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In light of the specification, it is clear that rising means holding gas that is produced through fermentation in dough, however, all flours are capable of holding some gas in their dough. It is clear from figures 23 and 24 that some doughs are capable of holding more gas than others; however, the current recitation of "rising" does not specify how much gas needs to be held in the dough for the flour from which it is made to be considered a "rising" flour. For the purpose of examination all flours will be interpreted to be "rising" flours, because all flours are capable of holding at least some gas in their dough.

Claim 1 recites the limitation "the transglutaminase" in line 2. There is insufficient antecedent basis for this limitation in the claim. The use of the article "the" implies that there is only one transglutaminase; and there are more than one transglutaminase enzymes known in the art.

The phrasing in lines 6 and 7 of claim 1 is awkward, and it is unclear if all allergenic amino acid sequences are eliminate or if only one allergenic amino acid sequence is eliminated. Because claim 3 recites single amino acid substitutions, it

appears that the elimination of a single sequence is encompassed by the claim. For the purpose of examination, the Examiner will interpret this recitation to be inclusive of a single amino acid substitution that eliminates one single allergenic epitope. This interpretation does not relieve the Applicant of the need to address this rejection under 35 USC 112, 2<sup>nd</sup> paragraph.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benmoussa et al (WO 00/18927, published on April 6, 2000) in view of Arentz-Hansen et al (J. Exp. Med. (2000) Vol. 191; pp. 603-612), further in view of Schuhmann, F. (US Patent No. 6,517,874, issued on Feb. 11, 2003, and published as US Pre-Grant Publication US 2002/0061344 on May 23, 2002), and further in view of Whitelam, G. C. (J. Sci. Food Agric. (1995) Vol. 68, pp. 1-9).

The claims are directed to a food flour derived from the seed of a non-wheat plant expressing transglutaminase and a wheat storage protein comprising SEQ ID NO:11; wherein the wheat storage protein has been modified by mutagenesis to eliminate an allergenic amino acid sequence; including wherein the sequence to be

modified is PFPQPQLPY (SEQ ID NO:36); and including wherein this sequence is modified at position 6; and including wherein the plant is rice, soybean or corn (also known as maize or *Zea mays*).

Benmoussa et al teach transgenic potato plants expressing wheat glutenin (see page 15). They specifically suggest multiple wheat storage proteins could be expressed in multiple starchy plant tissues; including the storage proteins glutenin, gliadin, albumin, and globulin (see abstract) and specifically including expression in maize (see abstract). They teach that the flours obtained by these starchy plants that have been transformed to express these wheat storage proteins can be used in applications that require increased viscosity and heat stability, and they specifically indicate that they are suitable for pastry- or bread-making (see entire document and page 10, lines 20-23); which indicates that these flours are rising flours.

Benmoussa et al do not teach mutagenesis to eliminate allergenic amino acid sequences. Benmoussa et al are silent with regard to allergenicity of their flours. Benmoussa et al do not teach plants expressing transglutaminase.

Arentz-Hansen et al teach mutagenesis of gliadin to render the gliadin less immunogenic; specifically generating synthetic peptides with a lysine residue substituted for the glutamine residue at position 63 or 65 of a peptide comprising PFPQPQLPY (same as the instant SEQ ID NO:36); and position 65 corresponds to position 6 in the instant SEQ ID NO:36 (see page 608 and Figure 4A). Arentz-

Hansen et al teach that this epitope is commonly recognized by the T-Cells of Celiac Disease patients (see page 608, right column).

Schuhmann teaches the addition of transglutaminase to flours, especially flours with low wheat content, to improve their dough properties, including retention of gas in the dough to result in an increase in bread volume (see column 2). Schuhmann teaches that the transglutaminase enzyme may be produced recombinantly (see column 4, lines 4-5).

Whitelam teaches that enzymes that are useful for processing of plant material can be produced recombinantly in the plants themselves (see introduction and pages 6 - 7). Whitelam specifically uses amylase and phytase as examples of such enzymes. In both of these cases the enzymes have traditionally been added to the plant material, but the experiments showed that they were successful in producing amylase and phytase in transgenic plants such that no exogenous enzyme would be required for processing (see pages 6-7).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the flours taught by Benmoussa et al to utilize transgenic seeds that expressed mutagenized gliadin that had reduced allergenicity for Celiac disease patients compared to wild-type gliadin. One would have been motivated to do so, because Arentz-Hansen et al teach that Celiac disease is the most common food sensitivity in humans (see introduction), and they specifically teach that substituting a lysine for the glutamine at the

position that corresponds to position 6 in the instant SEQ ID NO:36 is a substitution that eliminates T-Cell binding. Therefore, one of ordinary skill in the art would have appreciated that utilizing a gliadin coding sequence that was mutagenized to substitute lysine for glutamine at this position would have resulted in reduced allergenicity of the resulting flour for people with Celiac disease.

Benmoussa et al teach that glutenins and gliadins form inter-molecular cross-links that create a proteinaceous matrix which provides bread dough with viscoelastic properties (see lines 15-17 on page 1). Shuhmann teaches that transglutaminase generates new connections between the amino acids glutamine and lysine that are contained in the flour protein (see column 2, lines 55-58). At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Benmoussa et al and Arentz-Hansen et al with the teachings of Shuhmann and Whitelam to arrive at transgenic maize plants expressing both transglutaminase and a mutagenized gliadin. One would have been motivated to utilize the mutagenized gliadin for the reasons discussed above. One would have been motivated to include transglutaminase because Shuhmann teaches that adding transglutaminase to low-wheat flours improves the properties of dough made from such flours, and Whitelam teaches that one can grow processing enzymes in transgenic plants so that one would not have to add exogenous enzymes to the plant material for processing. One of ordinary skill in the art would have appreciated that by including expression of

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recombinant transglutaminase in the seeds that are also expressing gliadin, one would have been able to produce flour with improved dough properties that would not require addition of wheat or addition of transglutaminase enzyme.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/  
Primary Examiner, Art Unit 1638